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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,075	06/01/2001	Allan Svendsen	10038.200-US	4049

25908 7590 09/08/2004

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,075	SVENDSEN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-35,37-47,49-60 and 62-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-35,37-47,49-60,62,63,65 and 66* is/are rejected.

7)☒ Claim(s) *64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 12, 2004 has been entered.

The AF amendment filed March 11, 2004 canceling claims 36 and 61, adding claim 66 and amending claims 33, 37-42, 45-48, 58, 59 and 62-65 has been entered.

The amendment filed July 12, 2004 canceling claim 48 and amending claims 33, 35, 37-40, 47, 58-60 and 62-64 has been entered. It is noted that Applicants state that "claim 67 is added" ("Amendments to the claims" field July 12, 2004, page 2, 1st paragraph). However, there is no claim 67 in the current claim listing.

Claims 33-35, 37-47, 49-60 and 62-66 are pending.

Election/Restriction

During a telephone conversation with Mr. Jason Garbell on January 2, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1, 2, 4 (in part), 7 and 9-13, with election of species of A130. In view of election of species of A130, Group IV, claim 8, which also comprises A130, has been rejoined with Group I.

Applicant did not indicate which of the claims added by the amendment of August 11, 2003 are readable upon the elected species as required by MPEP 809.02(a).

Since no art has be found against species of A130, the search continued to other species recited in claim 33. Claims 49-52 and 54-57 have been rejoined.

Claim 59, with dependent claims 60 and 62-65, has been examined to the extent it reads on the species recited in claim 33. The species recited in claim 59 that are not within the species recited in claim 33, would have been restricted out and have not been examined. Thus, species such as Q1L/L2K/G8D/N15D, for example, have been withdrawn.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 3, line 4, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 34, 35, 37-47, 49-57, 59, 60 and 62-66 are objected to because of the following.

Claims 34, 35, 37-47, 49-57 and 66 depend from claim 33. Claim 33 is drawn to a cutinase variant while some dependent claims recite "the variant of claim 33", others (e.g., claim 40) recite "the cutinase variant of claim 33". It is noted that independent

claim 59 is drawn to a cutinase variant. Claims dependent thereon are drawn to the variant of claim 59. It is suggested that Applicants maintain consistency and use the same term in all claims.

Claims 41, 42 and 46 are objected to because there is no space between "in" and "SEQ ID NO:1".

In claims 35 and 60 "H. insolens" should be spelled out.

Claims 35 and 60 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 35 and 60 depend from claims 33 and 59, respectively. Claims 33 and 59 are drawn to a cutinase variant having "above 80% homology to SEQ ID NO:1". Claims 35 and 60 include limitation "wherein cutinase variant is a variant of the cutinase from H. insolens strain DSM 1800". Cutinase from H. insolens strain DSM 1800 has the amino acid sequence of SEQ ID NO:1.

Claim 59, with dependent claims 60 and 62-65, is objected as drawn to non-elected inventions.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-35, 37, 38, 40-47, 49-60, 62, 63, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cutinase variants comprising the specific mutations defined in the claims and having above 95% homology to SEQ ID NO:1, does not reasonably provide enablement for cutinase variants that have above 80%, 85% or 90% homology to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of cutinase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are

tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of the specific mutants (pages 25-26).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the great number of variants retain the claimed activity.

The specification does not support the broad scope of the claims which encompass cutinase variants with homology to SEQ ID NO:1 ranging from above 80% to above 90% because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting cutinase activity; (B) the general tolerance of cutinase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any cutinase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

It is noted that claim 58 is, in effect, drawn to a cutinase variant that has above 70% homology to SEQ ID NO:1.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a great number of substitutions in SEQ ID NO:1.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without necessary guidance, beyond that provided, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-35, 37-47, 49-58 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33, with dependent claims 34, 35, 37-47, 49-57, 66, is drawn to a cutinase variant comprising "a modification of at least one amino acid residue". The term "modification" may include chemical modification, for example. It is even more confusing because the dependent claims recite "substitutions". The specification refers to "specific substitutions" (page 5, line 12, for example). Claim 58 is confusing as reciting "differs by

"substitutions" and "comprises a modification". Amending the claims to use the term "substitution" would obviate this rejection.

Claims 41 and 42 are confusing as reciting "and/or" in Markush group.

Claim 45 recites the limitation "the parent cutinase". There is insufficient antecedent basis for this limitation in the claim.

Claim 46 (dependent from claim 41) is confusing as reciting "further comprising substitutions corresponding to E6Q + A14P + E47K + R51P + E179Q in SEQ ID NO:1" whereas claim 41 already recited "further comprising" said mutations.

Claim 47 (dependent from claim 33) is unclear because it recites "wherein the cutinase variant is a variant of a cutinase that has the amino acid sequence of SEQ ID NO:1". It is unclear how to distinguish between a variant of SEQ ID NO:1 that has above 80% homology to SEQ ID NO:1 and a variant of another sequence that has above 80% homology to SEQ ID NO:1. Further, claim 47 recites "substitutions corresponding to E6Q + A14P + E47K + R51P + A130V + E179Q" without indicating the sequence (SEQ ID NO:1).

Response to Arguments

Applicant's arguments filed July 12, 2004 have been fully considered.

With regard to the 112, 1st paragraph, enablement rejection, Applicants argue that "Foremost, the claimed cutinase variants are very structurally similar in that they possess above 80% homology to SEQ ID NO:1. As discussed in Applicants' prior response, based on this high degree of structural similarity, the artisan would

reasonably expect that the modifications recited in the claims and exemplified in the specification would be applicable to this genus of homologous structures" (Remarks, page 8). This is not persuasive because changing 20% percent of the cutinase structure would require extensive and undue experimentation based on the information provided by the specification. Applicants argue "the specification also provides an extensive disclosure of techniques which are which are well-known in the art for obtaining homologous structures and indeed it was routine for persons of ordinary skill in the art the time of the invention to prepare cutinase variants which possess above 80% homology to SEQ ID NO:1. See, e.g., the specification at page 2, lines 5-6, and the disclosure beginning at page 7 under the heading "Methods for Preparing Cutinase Variants." The specification also provides working examples exemplifying the ability of an artisan to produce and screen cutinase variants which possess above 80% homology to SEQ ID NO:1. See Examples 1-5" (page 8). This is not persuasive because the specification provides teachings regarding some specific substitutions in SEQ ID NO:1. Making the variant that is above 80% homologous would require introducing additional substitutions, effect of which on the function is unpredictable.

Applicants argue "The Office alleges that because the specification does not have appropriate guidance for producing cutinase variants having 80% homology to SEQ ID NO:1, that one of ordinary skill in the art would be reduced to producing and testing all of the virtually infinite possibilities. First, no where do the claims require (nor is it necessary for enablement) that the artisan "produce and screen all of the virtually infinite possibilities". Applicants are not suggesting that one skilled in the art go out and

make all of the possible cutinase variants falling within the claims. Rather, Applicants' specification and claims teach that the specification enables one skilled in the art to make and use the claimed sequences and clearly define the metes and bounds of the claimed invention" (page 9). This is not persuasive because the specification provides no sufficient guidance to distinguish between the substitutions within 20% of the cutinase structure that would not effect the requisite activity and the substitutions that would destroy said activity. Applicants argue that "the conclusion reached by the Patent Office that infinite screening and selection creates enablement problems can only be obtained by improperly associating undue experimentation with the time required for a task. However, the Federal Circuit long ago put an end to such conclusions, as the fact that a task may take time does not mean that the task involves undue experimentation. See *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Moreover, as of the time of the claimed invention, the time required for producing and screening massive variant libraries was insignificant, based on among other things, the advancement in computerized and robotic screening technology " (page 10). This is not persuasive because whether the time spent by one of ordinary skill in the art is significant or insignificant depends on the art technology. This time should correlate with the probability of obtaining the desired result. While In *in re Wands* the time spent on screening and thus obtaining the requisite product was predictable and the result was assured, making a cutinase variant having above 80% homology with SEQ ID NO: 1 would require extensive additional experimentation beyond the guidance provided by

the specification. Making variants with higher homology to SEQ ID NO:1 would significantly reduce said experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

September 2, 2004